## REMARKS

The Office Action and the cited and applied references have been carefully reviewed. Claims 1-10 presently appear in this application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claim 4 has been rejected under 35 U.S.C. §112, second paragraph, as being indefinite. This rejection is obviated by the amendment to claim 4, as supported by the present specification at page 12, lines 10-15.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claims 1-2 and 4-10 have been rejected under 35 U.S.C. \$102(e) as being anticipated by Hackett et al., US Patent 6,489,458. This rejection is respectfully traversed.

Claim 1 is amended to recite that the inverted repeat sequence comprises a sense strand sequence and an antisense strand sequence of a target nucleic acid and contains a mutation to be introduced into the target nucleic acid, wherein the sense strand sequence and the antisense strand sequence are arranged in tandem, and the mutation to be introduced into the target nucleic

acid is located within the sense strand sequence and the antisense strand sequence in the inverted repeat sequence in order to define the present invention more clearly. The amendment to claim 1 is supported by the present specification at page 8, lines 2-13 and 20-22, and in the Examples.

As is clear from amended claim 1, the mutation to be introduced into the target nucleic acid is located within the sense strand sequence and the antisense strand sequence in the inverted repeat sequence. For example, the inverted repeat DNAs specifically described in Example 2 in the specification have structures in which the nucleotides involved in repair of the mutant nucleotides are positioned in the sense strand sequence and the antisense strand sequence in the inverted repeat sequence as illustrated in Figure 1.

As disclosed in the passage of Hackett cited by the examiner (column 5, lines 45-52 of Hackett), a nucleic acid fragment comprising a nucleic acid positioned between at least two inverted repeats is used according to Hackett. This structure of the nucleic acid fragment is essential to Hackett's system because Hackett's method utilizes the activity of salmonid-type Tc1-like transposase (SB) protein to bind to inverted repeats in a transposon that flank an intervening

nucleic acid sequence and catalyze the incorporation of the transposon into DNA (column 9, lines 39-45, column 10, lines 55-60). In other words, the nucleic acid fragment according to Hackett must have the structure containing a nucleic acid of interest as an intervening nucleic acid sequence flanked by inverted repeats which are recognized and bound by the SB protein. Since the structure of the DNA having an inverted repeat sequence according to the presently claimed invention is different from the structure of the nucleic acid fragment according to Hackett as discussed above, the presently claimed invention is therefore not anticipated by Hackett.

The examiner further states that Hackett also teaches that the nucleic acid comprising IR integrates into the genome or target sequence by homologous recombination (page 5, lines 12-14 of the Office Action). However, Hackett, including the passage cited by the examiner, contains no disclosure concerning homologous recombination. In this connection, the examiner further alleges that Hackett teaches that his method can be used in transposon tagging (page 6, lines 12-19). In the passage of Hackett cited by the examiner (column 32, lines 4-33), it is disclosed that insertion in transposon tagging is approximately

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random. This also shows that the system of Hackett does not involve sequence-specific homologous recombination.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

Claim 4 has been rejected under 35 U.S.C. §103(a) as being unpatentable over Hackett et al., US Patent 6,489,458, in view of Dean et al., US Patent 6,130,207. Although claim 4 is indicated as being rejected over Hackett in view of Dean, it appears to applicants that the rejected claim should be claim 3 instead of claim 4. This rejection is respectfully traversed.

The system of Hackett requires the use of a transposase (or an SB protein) (column 5, lines 45-52, column 10, lines 55-60 Hackett). By contrast, the presently claimed method does not require the use of a transposase. Since the principle of Hackett's system is different from that of the presently claimed method, Hackett does not teach or suggest the presently claimed invention.

The sequences of the inverted repeats according to Hackett are restricted because each inverted repeat must contain a recognition site for the transposase (column 9, lines 39-45). By contrast, since there is no specific limitation concerning the target nucleic acid according to the presently claimed invention

as disclosed in the specification at page 7, lines 5-6, the inverted repeat sequence which comprises a sense strand sequence and an antisense strand sequence of the target nucleic acid can be designed at will. Thus, the effect of the presently claimed invention is unexpected to one of ordinary skill in the art reading Hackett and the presently claimed invention is furthermore advantageous over the subject matter of Hackett.

In addition, it should be noted that the examiner's interpretation of Hackett's disclosure at page 7, 2-5 lines from the bottom of the Office Action is inaccurate because Hackett contains no disclosure concerning homologous recombination in the passage cited.

Since Hackett does not teach or suggest the presently claimed invention, the presently claimed invention is not obvious over the combination of Hackett and Dean even if the secondary Dean reference teaches a plasmid comprising a DNA binding sequence specific for transcription factors as alleged by the examiner. Dean nevertheless does not satisfy the deficiencies noted for Hackett.

Reconsideration and withdrawal of the rejection are therefore respectfully requested.

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In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

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